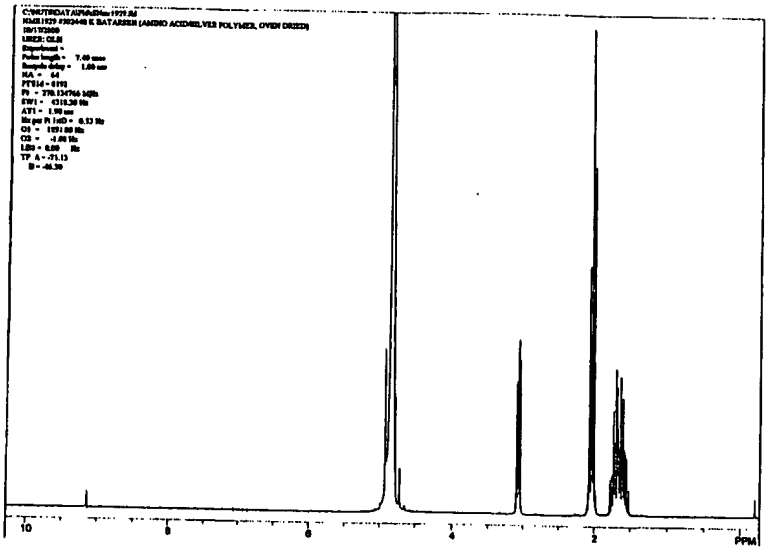
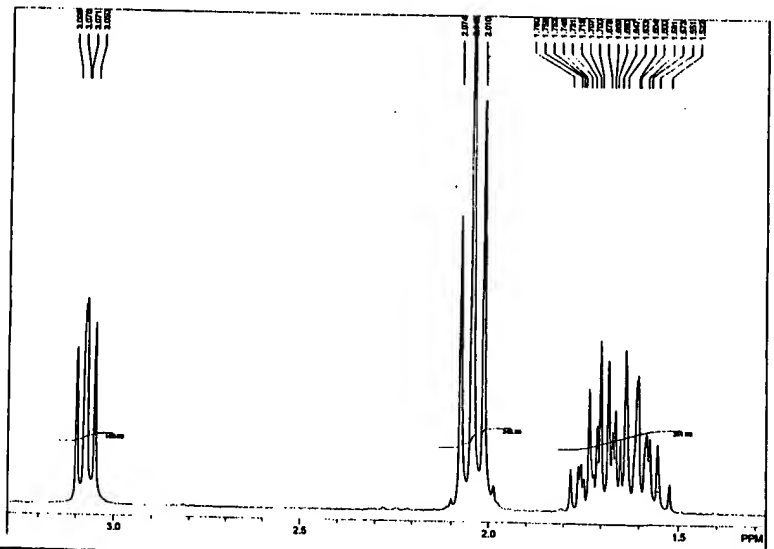




REMARKS

Reconsideration and continued examination of the above-identified application are respectfully requested.

The amendment further defines what the applicants regard as the invention. Full support for the amendment can be found throughout the present application, including the claims as originally

filed, for instance, at page 7, line 4 and claim 13 of the present application. Accordingly, no questions of new matter should arise and entry of the amendment is respectfully requested.

At page 2 of the Office Action, the Examiner rejects claim 28 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. The Examiner, for the most part, provides the same reasons for rejecting the claimed invention over 35 U.S.C. §112, second paragraph, as in the previous Office Action dated July 8, 2002. The Examiner also asserts that the figures are so small that they are impossible to read and the applicants have not shown how it is possible to combine one or more of the figures. For the following reasons, this rejection is respectfully traversed.

The figures of claim 28 relate to DSC spectrum, proton NMR spectrum, and carbon NMR spectrum. The carbon and hydrogen NMRs are distinct because they provide different information about the structure of the same solid. In addition, the DSC is also independent of both NMRs because it provides different information about the structure of the same solid. Page 15 of the present specification clearly defines DSC analysis and NMR analysis, which correspond to Figs. 1-3 of the present application. From page 15 of the specification, it is clear that Figs. 1-3 individually and/or collectively are the fingerprints of the product, and combining them is possible.

Additionally, the applicants have amended claim 28 to enlarge figures 1, 2, and 3 to better assist the Examiner. Accordingly, the rejection under 35 U.S.C. §112, second paragraph, should be withdrawn.

As stated in the previous response to the Office Action dated July 8, 2002, many of the references relied upon by the Examiner do not teach or suggest the use of any of the materials set forth in those references as a microbicidal composition. Accordingly, these references would not teach or suggest the claims relating to the use of the microbicidal compositions of the present

invention in controlling the growth of microorganisms or methods of controlling biofouling in a system. Moreover, the failure of the cited reference to teach or suggest the use of the composition as a microbicidal would also prevent an obviousness rejection with respect to combining references that show the addition of a disinfectant. It would not be obvious to one of ordinary skill in the art to include a disinfectant to the materials mentioned in a reference wherein that reference fails to teach or suggest the use of that material as a microbicidal composition. Thus, there would be no motivation for one having ordinary skill in the art to include a disinfectant when the composition mentioned in the reference does not even use the material for such microbicidal uses.

At page 3 of the Office Action, the Examiner rejects claims 1-4, 8, 11, 13, 16, 18, 21, 22, and 28 under 35 U.S.C. §102(b) as being anticipated by or, in the alternative, under 35 U.S.C. §103(a) as being obvious over Poddymov et al. or Sanchez et al. The Examiner, for the most part, provides the same reasons for rejecting the claimed invention over Poddymov et al. or Sanchez et al. as in the previous Office Action dated July 8, 2002. The Examiner asserts that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art. Further, with respect to the use of a disinfectant, the Examiner asserts that the cited art contains mixtures of the chelates and since the disinfectant is not defined by the claims, the mixture appears to fall within the scope of the claims. For the following reasons, this rejection is respectfully traversed.

Poddymov et al. and Sanchez et al. provide no structural spectrums. Poddymov et al. and Sanchez et al. merely provide values of acid dissociation constants and thermodynamic stability constants respectively. Additionally, the products of Poddymov et al. and Sanchez et al. are different from the claimed invention. According to pages 14 and 15 of the present application, the product of the claimed invention is in a solid state, while the references form stable complexes.

Furthermore, none of the references or the combination thereof, teaches or suggests that the soluble complexes can be used as antimicrobial agents. Additionally, the complex formation of Poddymov et al. occurs in glycine and aspartic acid solutions at a pH of greater than 6.5. The complex formation is increased by increasing the pH of the solution, while in the methionine solution, complexation decreases significantly below a pH of 3. Accordingly, the calculations for methionine were done at a pH of 4. In contrast, precipitation complexation of the claimed invention occurs at pH of equal or less than 2. Therefore, Poddymov et al. and Sanchez et al. do not teach or suggest the claimed invention. Accordingly, the rejection under 35 U.S.C. §102(b) or, in the alternative, under 35 U.S.C. §103(a) over Poddymov et al. or Sanchez et al. should be withdrawn.

At page 4 of the Office Action, the Examiner rejects claims 1-4, 7-16, 18-29, and 30 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gomori et al. (U.S. Patent No. 4,915,955) in view of Tsivion (International Publication Application No. WO 97/33477), Ackermann et al., Tumanov et al., Khurshid, Yamashita et al., Ali-Mohamed et al., Kawada et al., Modak et al. (U.S. Patent No. 5,708,023), Goodman and Gilman's, Poddymov et al. and Sanchez et al. The Examiner, for the most part, provides the same reasons for rejecting the claimed invention over Gomori et al. in view of Tsivion, Ackermann et al., Tumanov et al., Khurshid, Yamashita et al., Ali-Mohamed et al., Kawada et al., Modak et al., Goodman and Gilman, Poddymov et al. and Sanchez et al. as in the previous Office Action dated July 8, 2002. The Examiner also asserts that motivation exists to combine the references and that different products are formed at different pH levels as shown by Poddymov et al. and Sanchez et al. The Examiner further asserts that chelates are known to have biocidal activity and one skilled in the art would be motivated to combine products having biocidal activity to increase the spectrum and/or strength of the biocidal activity.

The Examiner states that every element of the invention has been collectively taught by the combined teachings of the references. For the following reasons, this rejection is respectively traversed.

The microbicidal composition of the claimed invention includes at least one disinfectant, a complex having at least one organic chelating moiety and at least one metal ion. Furthermore, the organic chelating moiety is present in at least an equimolar amount based on the amount of at least one metal ion, wherein the metal ion is microbicidal to at least one microorganism and the organic chelating moiety is an amino acid, wherein the amino acid includes a double bonded oxygen, and wherein the double bonded oxygen of the amino acid is complexed to M. The complex of the claimed invention is formed between the organic chelating moiety and the metal ion. Therefore, the metal ion is not in a solution. As further explained in the specification, the chelating moiety, which is formed from at least one amino acid, is chosen so as to make use of the lone pair of electrons on the nitrogen atom of the amino acid where the metal ion chelates with the nitrogen atom and the carbonyl group. This is what the applicants believe forms the complex, but the applicants do not wish to be held by this understanding only. In addition, the biocidal activity of the claimed invention results from the solubility of the organic chelating moiety portion of the complex in the biofilm of the microorganism, in which the metal ions are released intracellularly where they can exhibit their biocidal activities from within. Further, the applicants have shown in the application a preferred embodiment of this complex and its bioactivity.

Gomori relates to a disinfectant, which is formed when hydrogen peroxide is mixed with a concentrate. The concentrate contains silver, an inorganic acid, and an organic stabilizer. The organic stabilizer is preferably tartaric acid or citric acid. At columns 2 and 3 of Gomori, additional organic acid stabilizers are set forth. However, none of the acids set forth at columns

2 and 3 of Gomori are amino acids. The acids provided in Gomori are carboxylic acids and amides, and are not amino acids. Also, Gomori is not using the organic acid stabilizer as a biocide component, but simply as a stabilizer in order to be a UV protector for the hydrogen peroxide and silver, as emphasized by Gomori throughout the specification. The concentrate of Gomori is used to promote durability of the hydrogen peroxide. As such, for the reasons set forth above, Gomori does not teach or suggest the claimed invention.

In addition, the silver that is present in the concentrate of Gomori does not complex or form a complex with the organic acid stabilizer of Gomori. As indicated in the specification of Gomori, and in particular, column 3, lines 59-61, Gomori specifically indicates that if the ratio of hydrogen peroxide and silver is less than 1:99, "the possibility arises that the silver will precipitate from the admixture." This clearly implies that the silver is present in the solution and is not part of a complex. Gomori does not teach or suggest that the organic acids complex with Ag. Instead, Gomori shows that they are stabilizers to Ag (e.g., column 2, lines 37-38, 42-43, 65-66; column 6, lines 28-29). Also, Gomori indicates that the inorganic acids act as stabilizers for Ag as well, and not as complexes (column 3, lines 20-24).

In an effort to examine the effect of adding tartaric acid instead of glutamic acid on the silver solution, the applicants performed the following experiment. If helpful, upon the Examiner's request, the applicants will submit this experiment in the form of a 1.132 Declaration. The silver solution was prepared in accordance with the patent application. It was observed that if glutamic acid is added to the silver solution, then a yellowish precipitate is instantly observed, and if tartaric acid is added to the silver solution no precipitate is observed. This clearly ascertains the fact that the products of reactions for these systems are different, and therefore the solution equilibria are different as well.

Finally, Gomori does not teach or suggest that the concentrate alone acts as a disinfectant. In fact, Gomori indicates the complete opposite. According to Gomori, the concentrate of Gomori must be admixed with the hydrogen peroxide synergistically to form the disinfectant of Gomori. Clearly, according to Gomori, hydrogen peroxide is necessary. While the applicants appreciate that the claims as pending use the term "comprising", the applicants merely offer this comment to emphasize that Gomori is specifically teaching that the concentrate alone is not an effective disinfectant.

Further, Tsivion relates to combating fungal and bacterial pests in plants by using Al and/or Zn with either citric acid or a neutral amino acid glycine. No other metals are suggested and no basic or acidic amino acids are suggested. The pH is relatively high for the reaction conditions, unlike the claimed invention. Because the pH in Tsivion is relatively high, the chelation occurs between the metal and the coordinated oxygen atom. However, in the claimed invention, the chelation occurs between the metal and the uncoordinated oxygen atom of the carboxylic acid group. Moreover, unlike the claimed invention, which can be used on a broad spectrum of microorganisms and a plethora of applications, Tsivion is only used on plant pests. As such, for the reasons set forth above, Tsivion does not teach or suggest the claimed invention.

Ackermann et al. relates to the formation of compounds that result from the reaction of alkyl (CH_3-) and/or alkoxy (R-O) substituted phenylamine (C_6H_5-N) with halopropionic acids ($CH_3CH_2CO_2$-X wherein X = a halogen) and where the metal is chelated (Cu(II), Zn(II), Mn(II), Co(II), Mi(II), or Fe(II)/Fe(III)). Unlike the claimed invention, the starting material in Ackermann et al. is not an amino acid, but an amine. An amine is not an amino acid. Additionally, the metals of Ackermann et al. are not chelated with phenylalanine, but with phenylamines (which are not amino acids). Ackermann et al. does not teach or suggest antibacterial effects. Indeed, only

fungicide uses are mentioned. Accordingly, the rejection under 35 U.S.C. §102(b) or, in the alternative, under 35 U.S.C. §103(a) over Ackermann et al. should be withdrawn.

Tumanov et al. relates to the formation of complexes between Cu(II) and neutral alpha amino acids (glycine, alanine, and serine) where it can be used as bactericides. The only metal used is Cu(II). Additionally, no disinfectant is taught or suggested. Moreover, as shown in Tumanov et al., the chelation in Tumanov et al. occurs between Cu(II) and the coordinated oxygen atom, unlike the claimed invention where the chelation occurs between the metal and the uncoordinated oxygen atom of the carboxylic acid group. As such, for the reasons set forth above, Tumanov et al. does not teach or suggest the claimed invention.

Khurshid relates to the formation of amino acid complexes with Zn(II) and Fe(II) to be used as bactericides. The method of preparing the amino acid complex of Khurshid is shown in J.R.J. Sorenson (*J. Med. Chem., 19*) pp. 135-148, (1976), in which the preparation takes place in a basic environment (pg. 144, column 2, lines 18-19; "the solution to be weakly basic"). Moreover, no inorganic acid is used in forming the complex of Khurshid. Thus, unlike the claimed invention, the composition of Khurshid does not form a chelation between the metal and the uncoordinated oxygen atom of the carboxylic acid group.

Yamashita et al. relates to the formation of antibacterial substrates from N-(long-chain acyl RCO-) basic amino acids with Ag, Cu, or Zn under strong alkaline conditions. This solution is highly basic. Therefore, unlike the claimed invention where the chelation occurs between the metal and the uncoordinated oxygen atom of the carboxylic acid group, the chelation of Yamashita et al. occurs between the metal and the coordinated oxygen atom. As such, for the reasons set forth above, Yamashita et al. does not teach or suggest the claimed invention.

Ali-Mohamed et al. relates to the formation of Co(III) complexes with an organic dicarboxylic oxalate $^{-}OOC\text{-}COO^{-}$ and amino acids (glycine, alanine, or valine) to be used as bactericides. The chemical structure and constituents are totally different from the claimed invention. In essence, the Co coordinates with one nitrogen and three coordinated oxygen atoms (one from the amino acid and two from the oxalate), which is different from the claimed invention, which utilizes just amino acids, not an oxalate. Moreover, the only metal used in Ali-Mohamed is Co. Thus, for the reasons set forth above, Ali-Mohamed et al. does not teach or suggest the claimed invention.

Kawada et al. relates to the formation of complexes between neutral amino acids, such as methionine or pentocystine, with copper to control plant infections. Except for plants, there is no suggestion for these complexes to be used as bactericides. Further, the only metal used is Cu. Moreover, no disinfectants are taught or suggested. Moreover, unlike the claimed invention, where the coordination occurs between the metal and the uncoordinated oxygen atom of the carboxylic acid group, the chelation in Kawada et al. occurs between the metal and the coordinated oxygen atoms. Thus, for the reasons set forth above, Kawada et al. does not teach or suggest the claimed invention.

Modak et al. relates to the formation of a gel (not an insoluble complex) from zinc gluconate ($C_{12}H_{22}O_{14}Zn$), which is not an amino acid. The product of Modak et al. can be employed as a carrier for an irritant inactivating agent when applied to the skin or physical barriers. This gel does not bind to surfaces, especially skin, but forms a continuous film where the antimicrobial agent can be dispersed and distributed evenly so as to preclude these harmful chemicals from binding to the skin. Relatively soluble zinc and silver salts in Modak et al. are used to block binding sites on the skin, and the metals are <u>not</u> used as antimicrobial agents (column 6,

lines 61-67, and column 7, lines 1-5). Also, none of these soluble salts are of an amino acid complexation origin with either Zn or Ag. Moreover, contrary to the Examiner's suggestion, the zinc and the silver salts do not exhibit microbicidal activities (column 8, lines 52-55). Moreover, Modak et al. does not teach or suggest any other metals that can be used. Accordingly, the product of Modak et al. is a non-amino acid gel where it serves as a carrier to other disinfectants. Even though Modak et al. indicates the use of other disinfectants as described in Goodman and Gilman's "The Pharmacological Basis of Therapeutics," Mokak et al. does not teach or suggest adding these other disinfectants with metals that have been chelated with amino acids. As such, for the reasons set forth above, Modak et al. does not teach or suggest the claimed invention.

Goodman and Gilman's provides some antimicrobial reagents. However, Goodman and Gilman's does not teach or suggest that any of these reagents are metals chelated with amino acids. There is no teaching or suggestion that, when these compounds are combined with amino acids, they chelate to form disinfectants. As such, for the reasons set forth above, Goodman and Gilman's does not teach or suggest the claimed invention.

With respect to Poddymov et al. and Sanchez et al., as stated earlier, these two references do not teach or suggest the claimed invention. Specifically, they do not teach or suggest complexation occurring at a pH of less than or equal to 2.

Finally, the combination of all of the cited references relied upon by the Examiner does not teach or suggest the composition of the claimed invention wherein a chelation occurs between the metal and the uncoordinated oxygen atom of a carboxylic acid group and wherein the composition includes at least one disinfectant. Moreover, Poddymov et al. relates to determining the acid dissociation and Ag complexation constants and Sanchez et al. relates to determining the thermodynamic stability constant of Ag with phenylalanine, none of which teach or suggest a

complexation occurring at a pH level of less than or equal to 2. Additionally, some of the references, such as Tsivion, relate to combating fungal and bacterial pests in plants. Therefore, it is unlikely that one skilled in the art would combine these references, and even if one skilled in the art would combine the references, the combination of the references does not teach or suggest the claimed invention. Accordingly, the rejection under 35 U.S.C. § 103(a) over Gomori et al. in view Tsivion, Ackermann et al., Tumanov et al., Khurshid, Yamashita et al., Ali-Mohamed et al., Kawada et al., Modak et al., Goodman and Gilman's, Poddymov et al., and Sanchez et al. should be withdrawn.

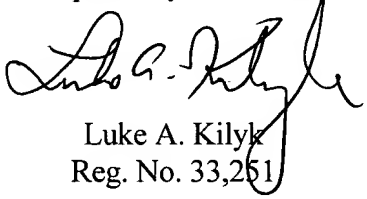
The Examiner is encouraged to contact the undersigned by telephone should there be any remaining questions concerning the allowability of claims as pending.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request the reconsideration of this application and the timely allowance of the pending claims.

If there are any other fees due in connection with the filing of this response, please charge the fees to Deposit Account No. 50-0925. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such extension is requested and should also be charged to said Deposit Account.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Twice Amended) A microbicidal composition comprising at least one disinfectant and a complex of the formula R-M, wherein R is at least one organic chelating moiety and M is at least one metal ion, and where R is present in an at least equimolar amount based on the amount of M, and M is microbicidal to at least one microorganism, wherein said at least one organic chelating moiety is an amino acid, wherein said amino acid includes a double bonded oxygen, and wherein said double bonded oxygen of said amino acid is complexed to M at a pH of about 2 or less.

9. (Twice Amended) A method to control the growth of microorganisms comprising contacting the microorganisms with a microbicidal composition comprising a complex of the formula R-M, wherein R is at least one organic chelating moiety and M is at least one metal ion, and where R is present in an at least equimolar amount based on the amount of M, and M is microbicidal to at least one microorganism, wherein said at least one organic chelating moiety is an amino acid, wherein said amino acid includes a double bonded oxygen, [and] wherein said double bonded oxygen of said amino acid is complexed to M at a pH of about 2 or less, and wherein said composition kills said microorganisms intracellularly.

16. (Twice Amended) A microbicidal composition comprising at least one disinfectant and a product obtained by combining, at least one metal ion (M) with at least an equimolar amount of at least one organic chelating moiety (R) based on the amount of M, wherein M is microbicidal to at least one microorganism, wherein said at least organic chelating moiety is an amino acid, wherein said amino acid includes a double bonded oxygen, and wherein said double bonded oxygen of said amino acid is complexed to M at a pH of about 2 or less.

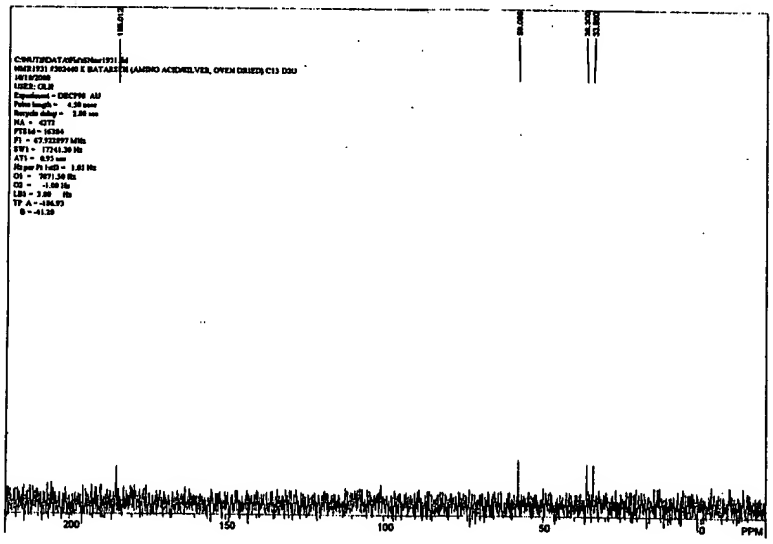
21. (Twice Amended) A microbicidal composition comprising a disinfectant and a complex of the formula R-M, wherein R is at least one organic chelating moiety and M is at least one metal ion, and where R is present in an at least equimolar amount based on the amount of M, and M is microbicidal to at least one microorganism, wherein said at least one organic chelating moiety is formed from an amino acid, and said organic chelating moiety has a carboxylic group which forms a dative covalent bond with M, and wherein said carboxylic group includes a double bonded oxygen which is complexed to M at a pH of about 2 or less.

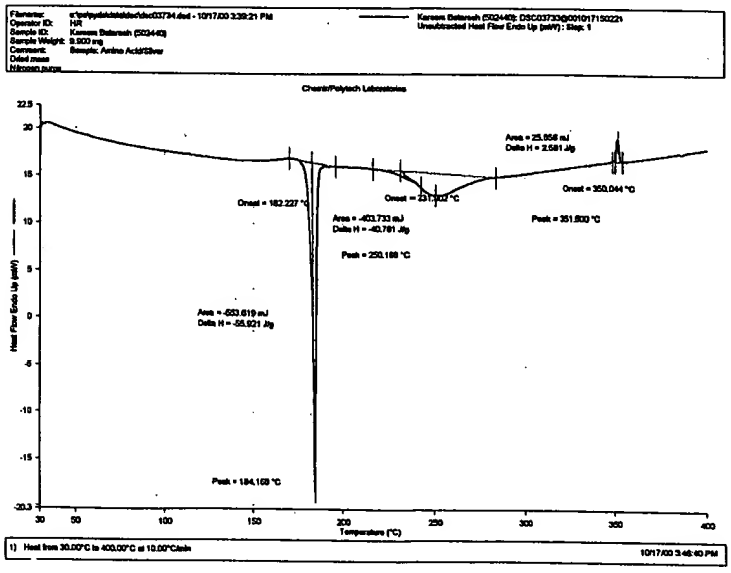
23. (Twice Amended) A method for preserving cut flowers or plants from pathological microorganisms comprising:

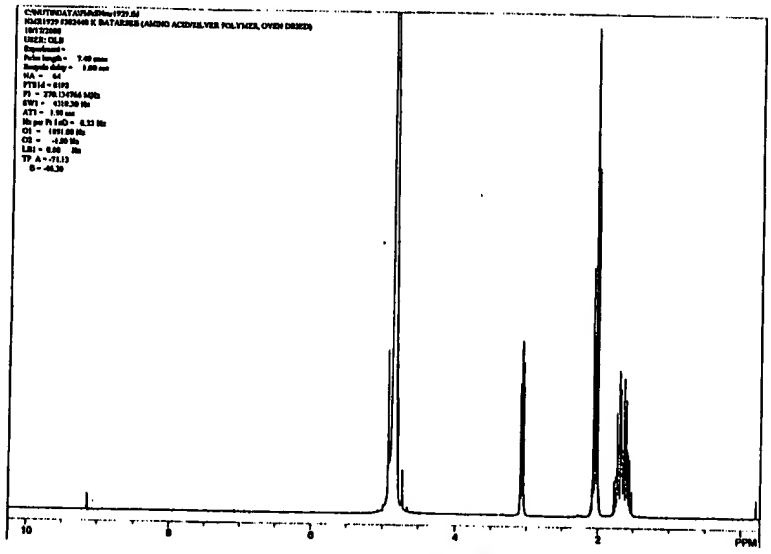
treating said flowers and plants with the microbicidal composition comprising a complex of the formula R-M, wherein R is at least one organic chelating moiety and M is at least one metal ion, and where R is present in an at least equimolar amount based on the amount of M, and M is microbicidal to at least one microorganism, wherein said at least one organic chelating moiety is an amino acid, wherein said amino acid includes a double bonded oxygen, and wherein said double bonded oxygen of said amino acid is complexed to M at a pH of about 2 or less.

26. (Twice Amended) A method for protecting living flowers or plants comprising treating said flowers and plants with the microbicidal composition comprising a complex of the formula R-M, wherein R is at least one organic chelating moiety and M is at least one metal ion, and where R is present in an at least equimolar amount based on the amount of M, and M is microbicidal to at least one microorganism, wherein said at least one organic chelating moiety is an amino acid, wherein said amino acid includes a double bonded oxygen, and wherein said double bonded oxygen of said amino acid is complexed to M at a pH of about 2 or less.

28. (Twice Amended) A microbicidal composition comprising an organo-metallic chelate of silver cations and glutamic acid, wherein the chelate exhibits the structural spectra depicted in Figures 1, 2, or 3, or combinations thereof below:



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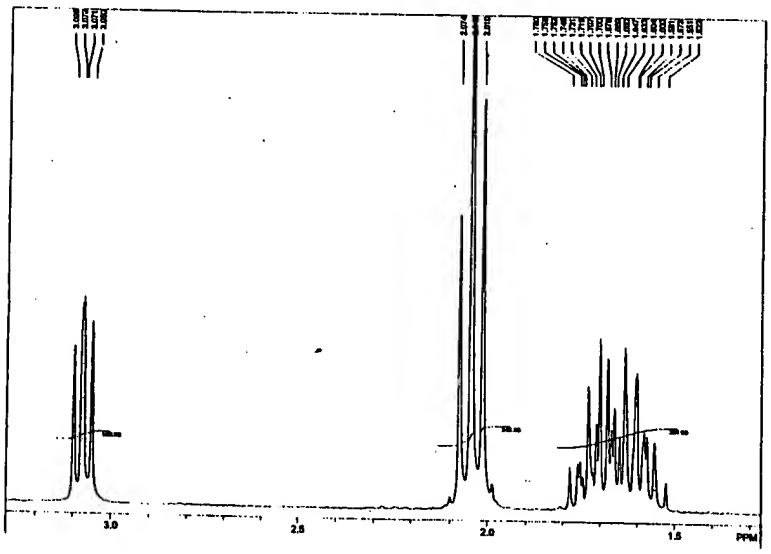
4
2
PPM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1.5
PPM